SARS-CoV-2 vaccines and donor recruitment for FMT

Due to its clear benefits in the management of recurrent *Clostridioides difficile* infection, faecal microbiota transplantation (FMT) has been advocated by the gastroenterological community as a non-postponable procedure to be continuously delivered during the COVID-19 pandemic.[1]

Therefore, specific recommendations have been released to reorganise the workflow of FMT during the pandemic to avoid the potential risk of transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) through the FMT procedure or the donor–recipient faecal transfer.[2] Briefly, these recommendations included the use of remote assessment of patients and donors whenever possible, the expansion of donor screening with questionnaires and laboratory testing aimed at excluding SARS-CoV-2 infection, and the application of specific safety measures during the endoscopic FMT procedure.[1,3]

The SARS-CoV-2 vaccination campaign has started worldwide in the past few weeks. One major category of vaccines (developed both by BioNTech and Pfizer, and also by Moderna and the National Institute of Allergy and Infectious Diseases) is based on mRNA products that encode a genetically modified SARS-CoV-2 spike protein. These vaccines are promising, with 93–95% efficacy and minimal side-effects. An additional emerging class of vaccines, that uses a non-replicating adenovirus vector with SARS-CoV-2 spike protein, including the ChAdOx1 nCoV-19 University of Oxford and AstraZeneca vaccine, has also been given at least temporary authorisation in some countries (eg, Argentina, Brazil, and the UK, among others). Finally, various vaccine technologies, including live attenuated vaccines, are being investigated.

Overall, these efforts are expected to give a considerable boost to the fight against COVID-19. Consequently, an important discussion in the field of human tissue transfer is required, and specifically in FMT. We must consider what effect vaccination will have on FMT in clinical practice based on current knowledge and data.

The first question is whether there should be a waiting period between SARS-CoV-2 vaccination and donor screening. In our latest consensus report on stool biobanking, a recent history (<2 months) of vaccination with a live attenuated virus was among the exclusion criteria for stool donors in case of a possible risk of transmission.[4] For vaccines based on mRNA technologies (rather than live attenuated virus), it does not seem feasible that there would be a risk for transmission, and this exclusion criterion can be disregarded, as already suggested for blood donors.[5] Nonetheless, available vaccines have been associated with some adverse events, including fatigue, nausea, fever, headache, myalgia, arthralgia, and pain at the injection site, among others, which can last several days after the vaccination. As these symptoms can overlap with those assessed during donor screening (at the entry questionnaire and the day of each donation), it might be pragmatic to wait 7–10 days from vaccination before evaluating potential donors to avoid the risk of inappropriate rejection of candidates. It could also be reasonable to follow such an approach for vaccines based on viral vectors, as suggested in UK blood donation guidelines.[6] Live attenuated virus vaccines are being developed and could become available for clinical use, but we still do not have data for risk of viral transmission with these candidate vaccines. Therefore, the safest approach might be to adhere to current guidelines for this type of vaccine and wait at least 2 months after vaccination before donor screening.[4] At the initial evaluation, all potential donor candidates should be asked about SARS-CoV-2 vaccination and, if vaccinated, a window of time (the length depending on the type of vaccine) should elapse before moving forward with full screening (appendix).

Another question is whether donors who have been vaccinated require clinical and laboratory investigations for COVID-19 during screening. Although it is recognised that current vaccines are effective in preventing COVID-19, uncertainty remains regarding their effect on transmission of the virus. More specifically, there are no available data for the presence of SARS-CoV-2 in the faeces of individuals who have been vaccinated if exposed, and of the risk of faecal–oral transmission of the virus. Finally, as we do not yet know how long vaccine immunity lasts, it would be difficult to predict the duration of the donor's protection against the virus. These open questions prevent any recommendation to change or streamline the current indications for the screening of stool donors, as current data do not yet assure us with a satisfactory level of safety for FMT.

Irrespective of the above considerations, because different steps of the FMT process (eg, the evaluation of donors and patients, the manipulation of faeces, the FMT procedure itself, and the follow-up of patients) could expose donors, patients, and physicians to SARS-CoV-2 infection, it is reasonable and wise to strongly encourage vaccination.

In conclusion, although the roll-out of vaccines is expected to be a turning point in the pandemic, the alert level applied to the FMT workflow to prevent the transmission of SARS-CoV-2 cannot be reduced until further data emerges.

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1 Ianiro G, Mullish BH, Kelly CR, et al. Screening of faecal microbiota transplant donors during the COVID-19 outbreak: suggestions for urgent updates from an international expert panel. *Lancet Gastroenterol Hepatol* 2020; **5:** 430–32.

2 Xiao F, Tang M, Zheng X, Liu Y, Li X, Shan H. Evidence for gastrointestinal infection of SARS-CoV-2. *Gastroenterology* 2020; **158:** 1831–33.

3 Ianiro G, Mullish BH, Kelly CR, et al. Reorganisation of faecal microbiota transplant services during the COVID-19 pandemic. *Gut* 2020; **69:** 1555–63.

4 Cammarota G, Ianiro G, Kelly CR, et al. International consensus conference on stool banking for faecal microbiota transplantation in clinical practice. *Gut* 2019; **68:** 2111–21.

5 EUR-Lex. Commission Directive 2004/33/EC of 22 March 2004 implementing Directive 2002/98/EC of the European Parliament and of the Council as regards certain technical requirements for blood and blood components. 2015. https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32004L0033 (accessed Jan 14, 2021).

6 NHS Blood and Transplant. Coronavirus: latest advice. 2020. https://www.blood.co.uk/news-and-campaigns/news-and-statements/coronavirus-covid-19-updates/ (accessed Jan 14, 2021).